8. REGULATIONS AND ADVISORIES

The international and national regulations and guidelines regarding xylenes in air, water, and other media are summarized in Table 8-1.

ATSDR has derived inhalation and oral MRLs that apply to mixed xylenes and the individual isomers. An acute-duration inhalation MRL of 2 ppm is based on a minimal LOAEL of 50 ppm (217 mg/m^3) for mild objective and subjective respiratory effects and subjective neurological effects in subjects exposed to *m*-xylene vapor for 2 hours (Ernstgard et al. 2002); an uncertainty factor of 30 was applied to the minimal LOAEL. An intermediate-duration inhalation MRL of 0.6 ppm is based on a minimal LOAEL of 50 ppm (217 mg/m^3) for a small decrease in the latency of the paw-lick response in male rats exposed to *m*-xylene vapor 6 hours/day, 5 days/week for 3 months (Korsak et al. 1992); an uncertainty factor of 90 was applied to the human equivalent minimal LOAEL. A chronic-duration inhalation MRL of 0.05 ppm is based on a LOAEL of 14 ppm (geometric mean) for mild subjective respiratory and neurological symptoms in workers exposed to 70% xylene 8 hours/day, 5 days/week for 1–7 years (Uchida et al. 1993); an uncertainty factor of 100 and modifying factor of 3 was applied to the LOAEL. An acute-duration oral MRL of 1 mg/kg/day is based on a NOAEL of 125 mg/kg and a LOAEL of 250 mg/kg for alteration of visual evoked brain potentials in rats exposed to *p*-xylene for 45 minutes (Dyer et al. 1988); an uncertainty factor of 100 was applied to the NOAEL. An intermediate-duration oral MRL of 0.4 mg/kg/day is based on a NOAEL of 500 mg/kg/day (duration-adjusted, 360 mg/kg/day) and a LOAEL of 1,000 mg/kg/day (duration-adjusted, 710 mg/kg/day) for hyperactivity in mice immediately after oral gavage dosing with mixed xylene (plus 17% ethylbenzene) 5 days/week during weeks 4–51 of a 2-year study (NTP 1986); an uncertainty factor of 100 was applied to the duration-adjusted NOAEL. In addition, a modifying factor of 10 was applied to account for the lack of testing for sensitive neurological effects and lack of developmental and multi-generational data. A chronic-duration oral MRL of 0.2 mg/kg/day is based on a NOAEL of 250 mg/kg/day (duration-adjusted, 179 mg/kg/day) for the lack of any overt neurological toxicity or systemic toxicity in rats that received oral gavage doses of mixed xylene (plus 17% ethylbenzene) 5 days/week for 2 years (NTP 1986); an uncertainty factor of 100 was applied to the duration-adjusted NOAEL of 179 mg/kg/day. In addition, a modifying factor of 10 was applied for the lack of testing for sensitive neurological end points and lack of developmental and multi-generational data. Specific details about the MRL derivations are in Appendix A.

EPA (IRIS 2005) has derived an inhalation reference concentration (RfC) for mixed xylenes of 0.1 mg/m^3 (0.02 ppm) based on a NOAEL of 50 ppm (217 mg/m^3) and a LOAEL of 100 ppm (434 mg/m^3) for

Table 8-1. Regulations and Guidelines Applicable to Xylenes

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines:			
IARC	Carcinogenicity classification	Group 3[a]	IARC 2004
WHO	Air quality guidelines	No data	WHO 2000
	Drinking water quality guidelines	0.5 mg/L[b]	WHO 2004
NATIONAL			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (TWA)	435 mg/m^3	ACGIH 2004
	STEL	655 mg/m^3	
EPA	Hazardous air pollutant (isomers and mixture)	Yes	EPA 2004b 42 USC 7412
NAS/NRC	AEGL-1[c]		EPA 2007
	10, 30, and 60 minutes, 4 and 8 hours	130 ppm	
	AEGL-2[c]		
	10 minutes	2500 ppm[d]	
	30 minutes	1300 ppm[d]	
	60 minutes	920 ppm[d]	
	4 hours	500 ppm	
	8 hours	400 ppm	
	AEGL-3[c]		
	10 minutes	7,200 ppm[e]	
	30 minutes	3,600 ppm[d]	
	60 minutes	2,500 ppm[d]	
	4 hours	1,300 ppm[d]	
	8 hours	1,000 ppm[d]	
NIOSH	REL (15-minute ceiling limit)	435 mg/m^3	NIOSH 2005
	IDLH	3,906 mg/m^3	
	STEL	655 mg/m^3	
OSHA	PEL (8-hour TWA) for general industry	435 mg/m^3	OSHA 2005c 29 CFR 1910.1000
	PEL (8-hour TWA) for construction industry	435 mg/m^3	OSHA 2005b 29 CFR 1926.55
	PEL (8-hour TWA) for shipyard industry	435 mg/m^3	OSHA 2005a 29 CFR 1915.1000
b. Water			
EPA	Designated as hazardous substances in accordance with Section 311(b)(2)(A) of the Clean Water Act	Yes	EPA 2005b 40 CFR 116.4

Table 8-1. Regulations and Guidelines Applicable to Xylenes

Agency	Description	Information	Reference
NATIONAL *(cont)*			
EPA	Drinking water standards and health advisories		EPA 2004a
	1-day HA (10-kg child)	40 mg/L	
	10-day HA (10-kg child)	40 mg/L	
	DWEL	7.0 mg/L	
	National primary drinking water standards (total xylenes)		EPA 2002b
	MCLG	10 mg/L	
	MCL	10 mg/L	
	Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act	100 pounds	EPA 2005c 40 CFR 117.3
c. Food			
EPA	Exemption from the requirement of a tolerance		EPA 2005f 40 CFR 180.1025
	Xylenes applied as an emulsion	Initial concentration not to exceed 750 ppm	
	Maximum residue of xylenes in potable water system/return flows of treated irrigation water into receiving rivers and streams	10 ppm	
FDA	Bottled drinking water	10 mg/L	FDA 2006 21 CFR 165.110
d. Other			
ACGIH	Carcinogenicity classification	A4[f]	ACGIH 2004
	Biological exposure indices	1.5 g/g creatinine	
	Methylhippuric acids in urine (end of shift)		
EPA	Carcinogenicity classification	Data are inadequate for an assessment of the carcinogenic potential	IRIS 2005
	Inhalation unit risk	Not applicable	
	Oral slope factor	Not applicable	
	RfC	0.1 mg/m^3	
	RfD	0.2 mg/kg/day	

Table 8-1. Regulations and Guidelines Applicable to Xylenes

Agency	Description	Information	Reference
NATIONAL *(cont)*			
EPA	Superfund, emergency planning, and community right-to-know		
	Designated CERCLA hazardous substance		EPA 2005d 40 CFR 302.4
	Reportable quantity		
	Xylenes and *p*-xylenes	100 pounds	
	m-Xylenes and *o*-xylenes	1,000 pounds	
	Effective date of toxic chemical release reporting	01/01/87	EPA 2005e 40 CFR 372.65
NTP	Carcinogenicity classification	No data	NTP 2005

[a]Group 3: Not classifiable as to carcinogenicity to humans
[b]Concentrations of the substance at or below the health-based guideline value may affect the appearance, taste, or odor of the water, leading to consumer complaints.
[c]AEGL-1 is the airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic nonsensory effects. AEGL-2 is the airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape. AEGL-3 is the airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death.
[d]Values denoted as having safety considerations against the hazard of explosion; the Lower Explosive Limit (LEL)=9,000 ppm and each value should be $\geq$10% LEL. Safety considerations against the hazard(s) of explosion(s) must be taken into account.
[e]Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.
[f]A4: Not classifiable as a human carcinogen

ACGIH = American Conference of Governmental Industrial Hygienists; AEGL = acute exposure guideline level; CERCLA = Comprehensive Environmetnal Response, Compensation, and Liability Act; CFR = Code of Federal Regulations; DWEL = drinking water equivalent level; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; HA = health advisory; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Informatin System; MCL = maximum contaminant level; MCLG = maximum contaminant level goal; NAS/NRC = National Academy of Sciences/National Research Council; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; STEL = short-term exposure limit; TLV = threshold limit values; TWA = time-weighted average; USC = United States Code; WHO = World Health Organization

impaired motor coordination (decreased rotarod performance) in male rats exposed to *m*-xylene vapor 6 hours/day, 5 days/week for 3 months (Korsak et al. 1992); an uncertainty factor of 300 was applied to the NOAEL. EPA (IRIS 2005) has derived an oral reference dose (RfD) for mixed xylenes of 0.2 mg/kg/day, based on a NOAEL of 250 mg/kg/day and a LOAEL of 500 mg/kg/day for dose-related decrease in body weight and increase in mortality in male rats treated by oral gavage 5 days/week for 2 years (NTP 1986); an uncertainty factor of 1,000 was applied to the NOAEL.